In conversation with... iConsensus

10 October 2023

innovative health initiative

How to make a more efficient, cost-effective and user-friendly process for the development and manufacture of biopharmaceuticals

innovative health initiative

In conversation with... iConsensus

Meet the speakers

Veronique Chotteau

Coordinator of the iConsensus project

Associate Professor of Industrial Biotechnology

KTH

Luc Kupers

Project Leader of iConsensus - Technical

Former MSAT Fellow Innovation

Sanofi

Fabien Abeille

Co-coordinator of iConsensus and leader of work on system automation & integration, and data monitoring & management

Senior R&D Scientist

Micronit

Åsa Emmer

Leader of iConsensus work on the capillary electrophoresis-chip platform

Professor in Analytical Chemistry

KTH

Aman Russom

Leader of the iConsensus work on affinity-based, microfluidics and holographic methods

Professor of Nanobiotechnology

KTH

Marc Dietrich Voss

Project Leader of iConsensus - Management

Director Global Alliance Management Public-Private Partnerships

Sanofi

Salomé Koussoroplis

Scientific Project Officer

Innovative Health Initiative

COCIR efpia EuropaBio MedTech Europe from diagnosis to cure Vaccines Europe Co-funded by the European Union

innovative health initiative

In conversation with... iConsensus

Agenda

14:00-14:10 Introduction and welcome
14:10-15:25

- Challenges and objectives
- Tangible results and their impact
- Exploitation of results and sustainability of assets developed

15:25-15:30 Closing remarks

The session will focus on a project supported by the Innovative Medicines Initiative (IMI), a partnership between the European Union and the European pharmaceutical industry.

COCIR efpia EuropaBio MedTech Europe from diagnosis to cure Vaccines Europe Co-funded by the European Union

innovative health initiative

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Use the chat below

Ask questions and interact with the speakers
(bottom of your screen)

The session is being **recorded.**
The recording will be posted on IHI's website and Youtube channel.

COCIR efpia EuropaBio MedTech Europe Vaccines Europe Co-funded by the European Union

innovative health initiative

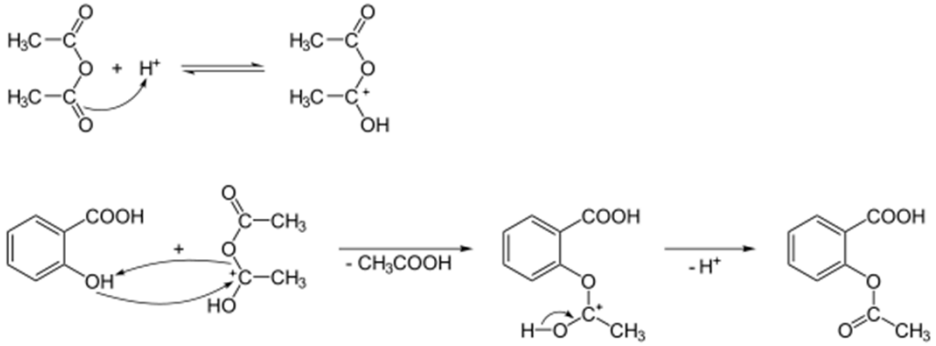
Creating a sensing platform for biopharmaceutical cultivation process and high-throughput system

Assoc. Prof. Veronique Chotteau, KTH
Dr. Luc Kupers, former Sanofi
Dr. Marc Dietrich Voss, Sanofi
Dr. Fabien Abeille, Micronit
Prof. Åsa Emmer, KTH
Prof. Aman Russom, KTH

Challenges and objectives

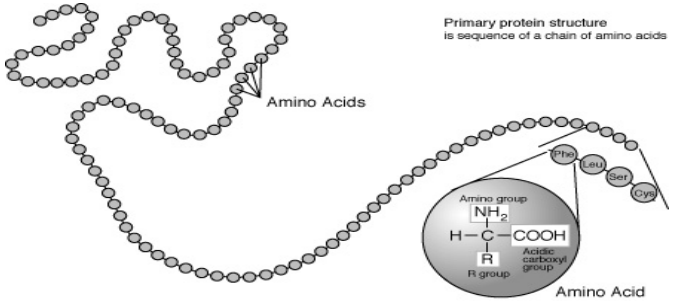
Pharma small molecule

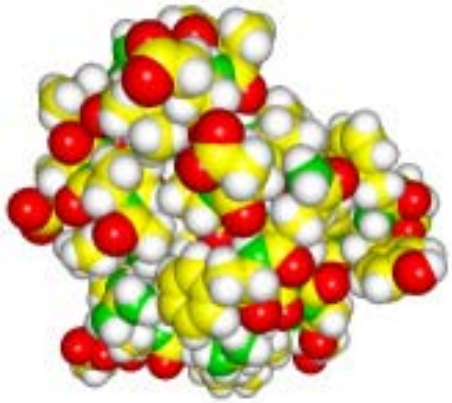
- Aspirin production is a chemical reaction
- Tons per day



Biopharmaceutical

- A protein is a chain of amino acids.
- Kg's per year



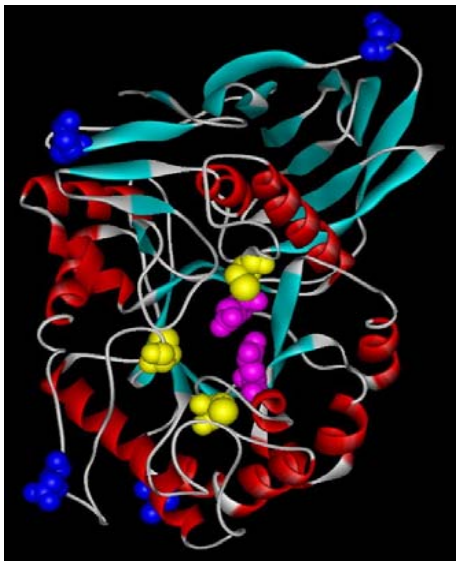


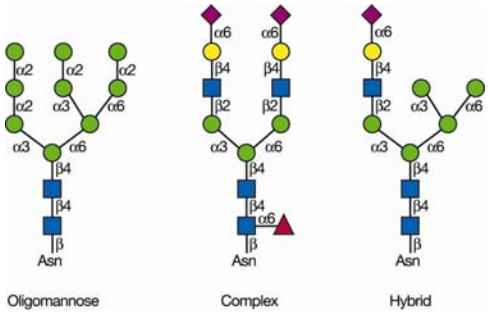
Biopharmaceuticals

large molecular weights	high structural complexity
heterogeneous ≠ molecular species	heterogeneous impurity profile
sensitive to physical conditions	bio-assays
master cell banks	post-translational modifications

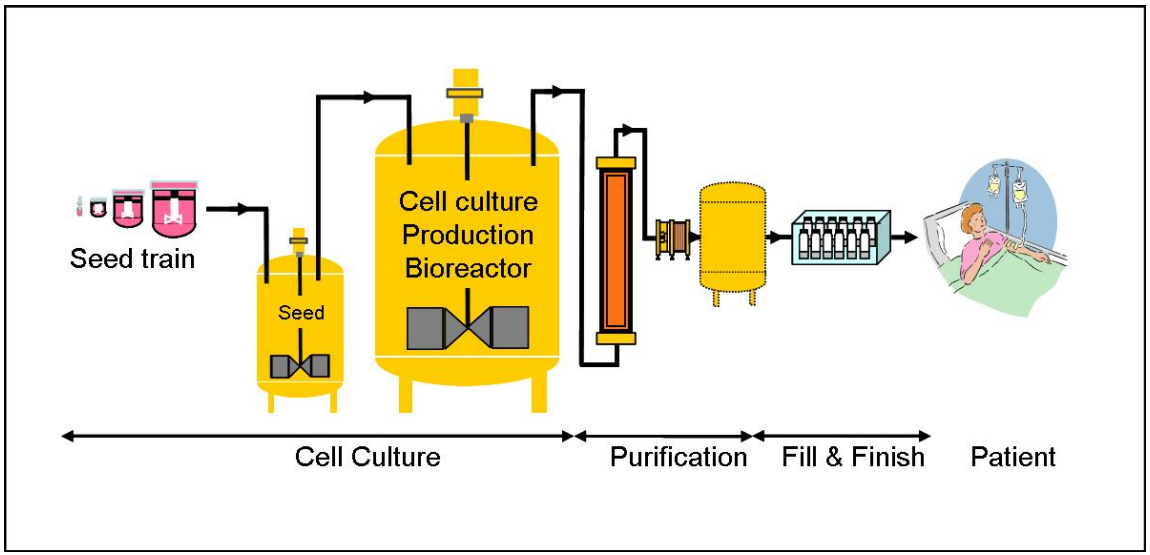
PTM: Glycosylation

- Correct folding
- Potency
- Effector functions
- Receptor binding
- Immunogenicity
- Pharmacokinetics
- Stability





The production of biopharmaceuticals



ACTIP

The Advanced Cell Technology Industrial Platform (ACTIP)

ACTIP is an independent non-profit association of European companies and institutions engaged in the industrial use of advanced cell technology for research, development and/or production of biopharmaceuticals, vaccines and other preventative or therapeutic approaches.

Its main objectives are to bring advanced cell technology experts together for networking, keeping up to date on cutting-edge developments and focus on technological and applied-oriented challenges for the industrial use of advanced cell technology.

ACTIP Position Paper

2012 drafted position paper for the EU

Way to Strategic Research Agenda

Visit in 2012 to the DG R&D accompanied by Hansjorg Hauser, Chairman of ESACT

…directed us towards the IMI2-program

Contacted Executive Director Science Policy & Regulatory Affairs at **EFPIA**

Strategic Research Agenda for biomedical research

Strategic Research Agenda

The right prevention and treatment for the right patient at the right time
Outline Strategic Research Agenda for a biomedical research public private partnership under Horizon 2020

July 2013
Strategic Research Agenda for biomedical research

needed for their utilisation initiating formal consultation as required.

- The development of predictive pre-clinical tools for toxicity and/or immunogenicity to reduce the risk of failure in clinical trials. ~~Develop a better understanding of the~~
- Conduct the basic research and develop the tools required to support the development of innovative preventative medicines for disease of high societal impact
- Implementation of new approaches for the development and production of biopharmaceuticals, vaccines, cell-based therapies, tissue engineering, gene therapies, preventive medicines or more rapid diagnostics
- Where co-investment is justified based on societal and healthcare need, and there are sufficient validated tools available, jointly develop novel therapeutic agents and disease prevention strategies
- Conduct research required to support the establishment of the necessary regulatory pathways and frameworks and payer framework to support the authorisation of new preventative medicines (driven under axis 2)
- Conduct research in manufacturing technology to produce the innovative medicines through highly flexible and cost-effective processes that guarantee high quality and safety.
- Develop new simple and robust process and product analytical tools to assure highly controlled and safe production processes, including effective methods to detect and prevent adventitious agent contaminations.
- Develop and/or optimize vaccine/protein formulation and conduct more research for the right excipients that increase stability, especially with regard to proteins and the new and complex multivalent vaccines.
- Provide improved access to information and support allowing individuals to make more

Why public-private cooperation?

Industry

Standardized GMP-processes

Technology development not core business

Academia & SMEs

Innovation drivers

Focus on new technologies

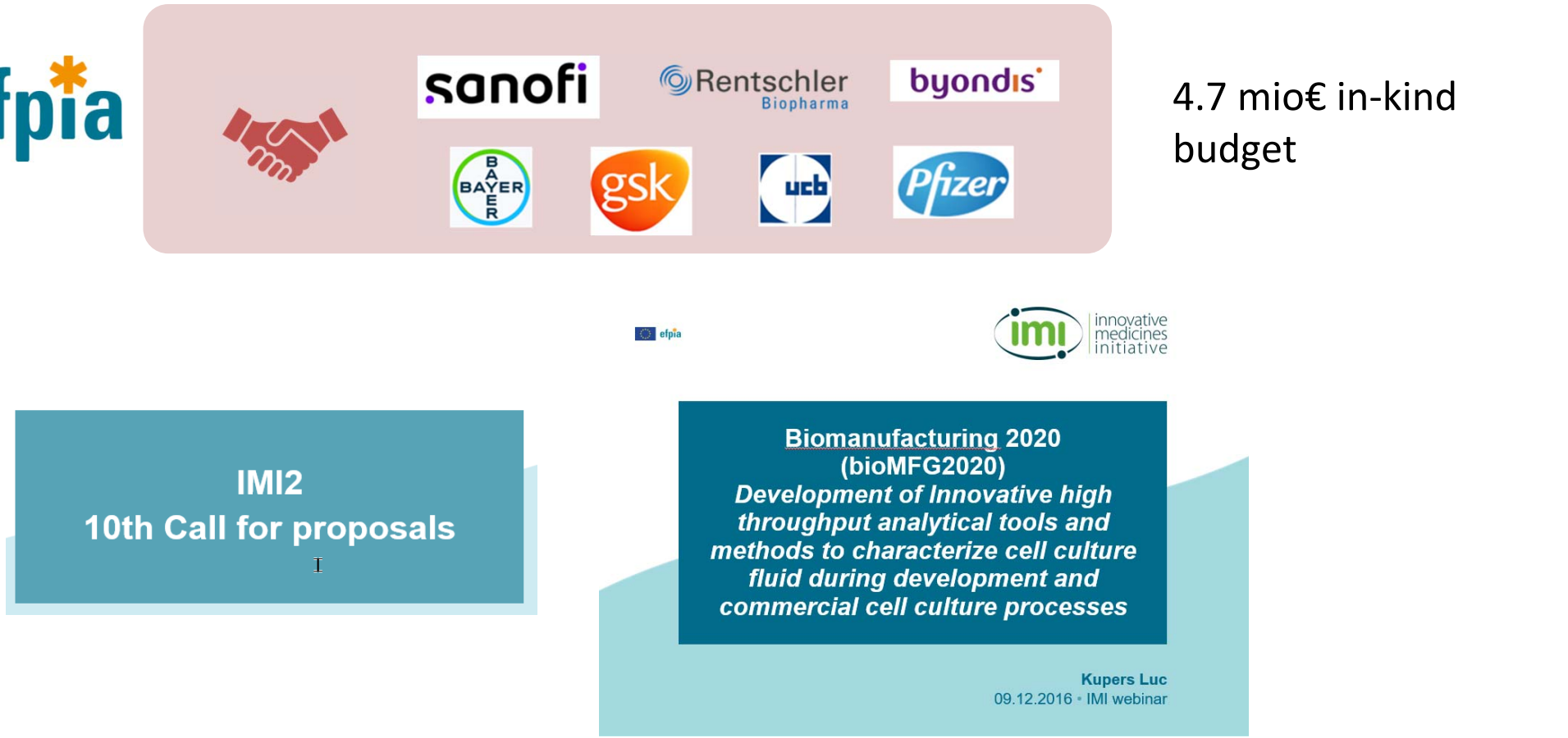
Need for heterogenous and complementary collaboration partners

Leveraging existing networks of public partners: trust & capabilities

→ Innovative Medicines Initiative

Building industry consortium and Call 10 launch

4.7 mio€ in-kind budget



Stage 1

10 Expressions of interest:

- Scientific expertise
- Complementary technological assets and capabilities
- Academic institutes and heterogenous SMEs represented
- Previous experience with public private partnerships

iConsensus selected

Integrated control and sensing platform for biopharmaceutical cultivation process high-throughput development and production

Full project proposal and grant agreement

2017

Topic: IMI2-2016-10-05

Type of action: IMI2-RIA
(Research and Innovation action)

Proposal number: 777397-2

Proposal acronym: iConsensus

Deadline Id: H2020-JTI-IMI2-2016-10-two-stage

Full Proposal

2018

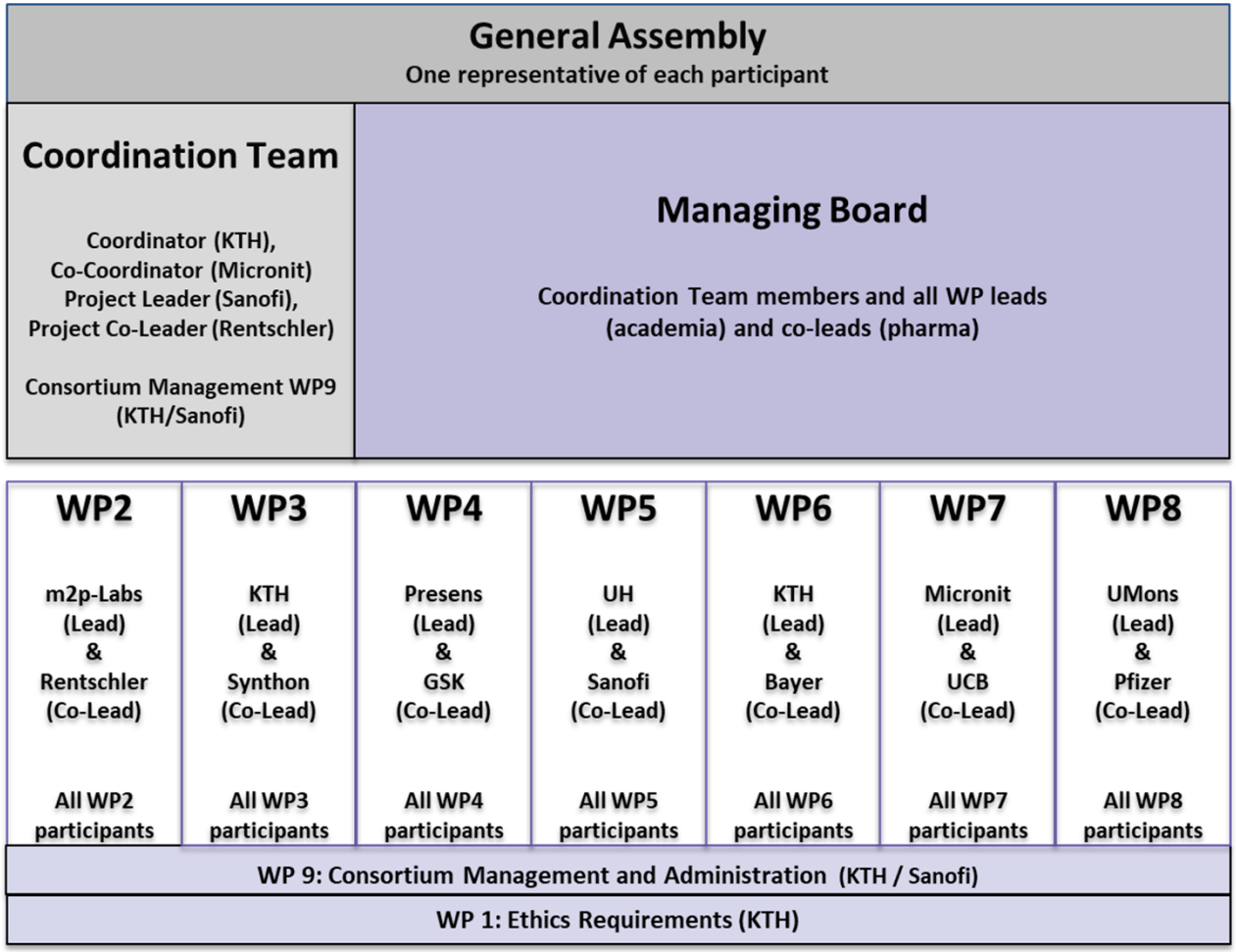
Innovative Medicines Initiative 2
Joint Undertaking (IMI 2 JU)

Multi-beneficiary Model Grant Agreement

(IMI 2 JU MGA — Multi)

Innovative Medicines Initiative 2 Joint Undertaking
[grant agreement No 777397]

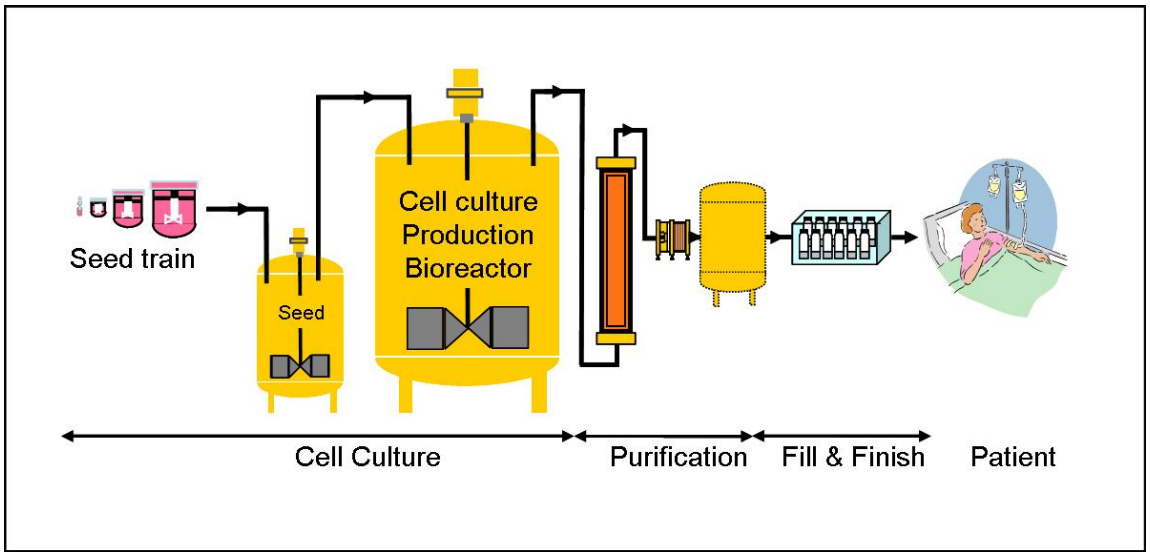
Negotiation of consortium agreement and governance



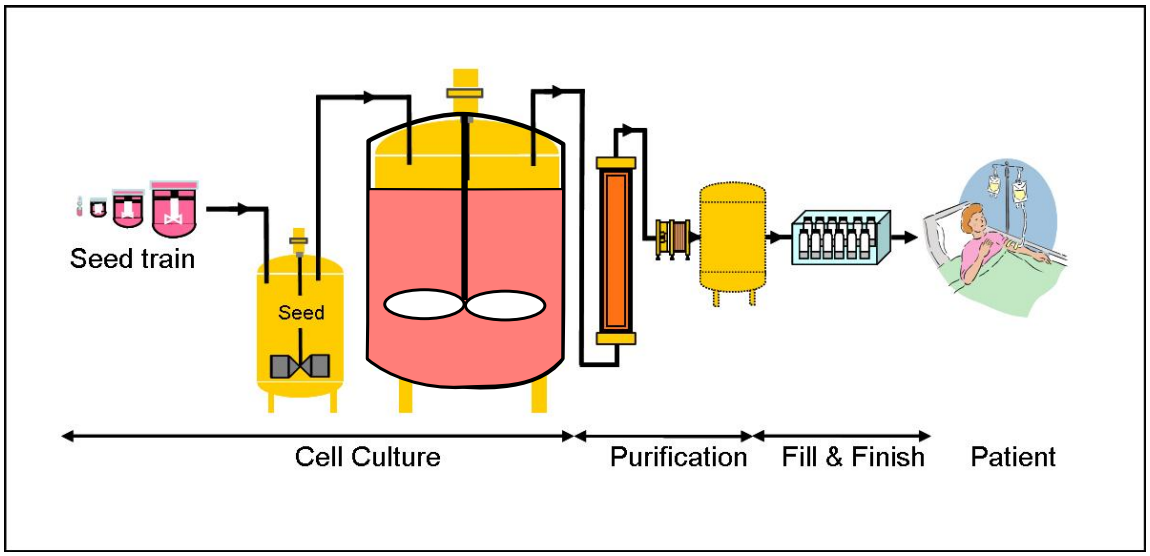
28 May 2018
iConsensus
1st plenum meeting and start of the project

Tangible results and their impact

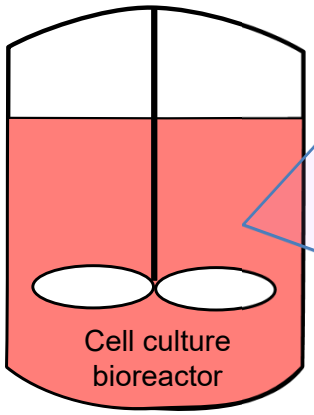
iConsensus – The Project



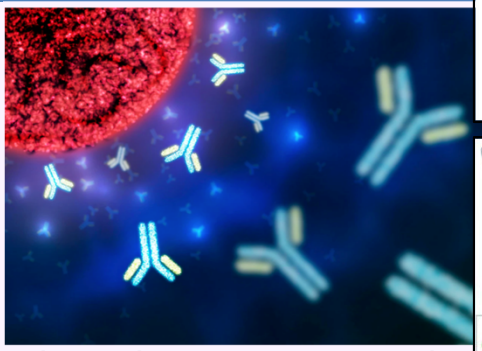
iConsensus – The Project

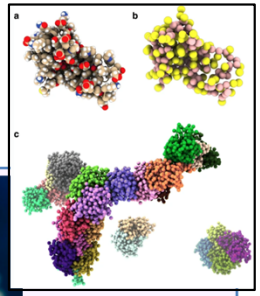


iConsensus – The Project



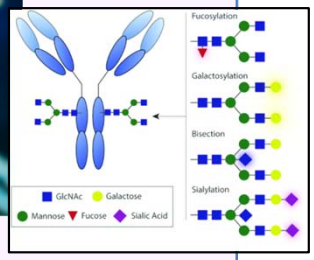
cells





Correct quality

aggregation



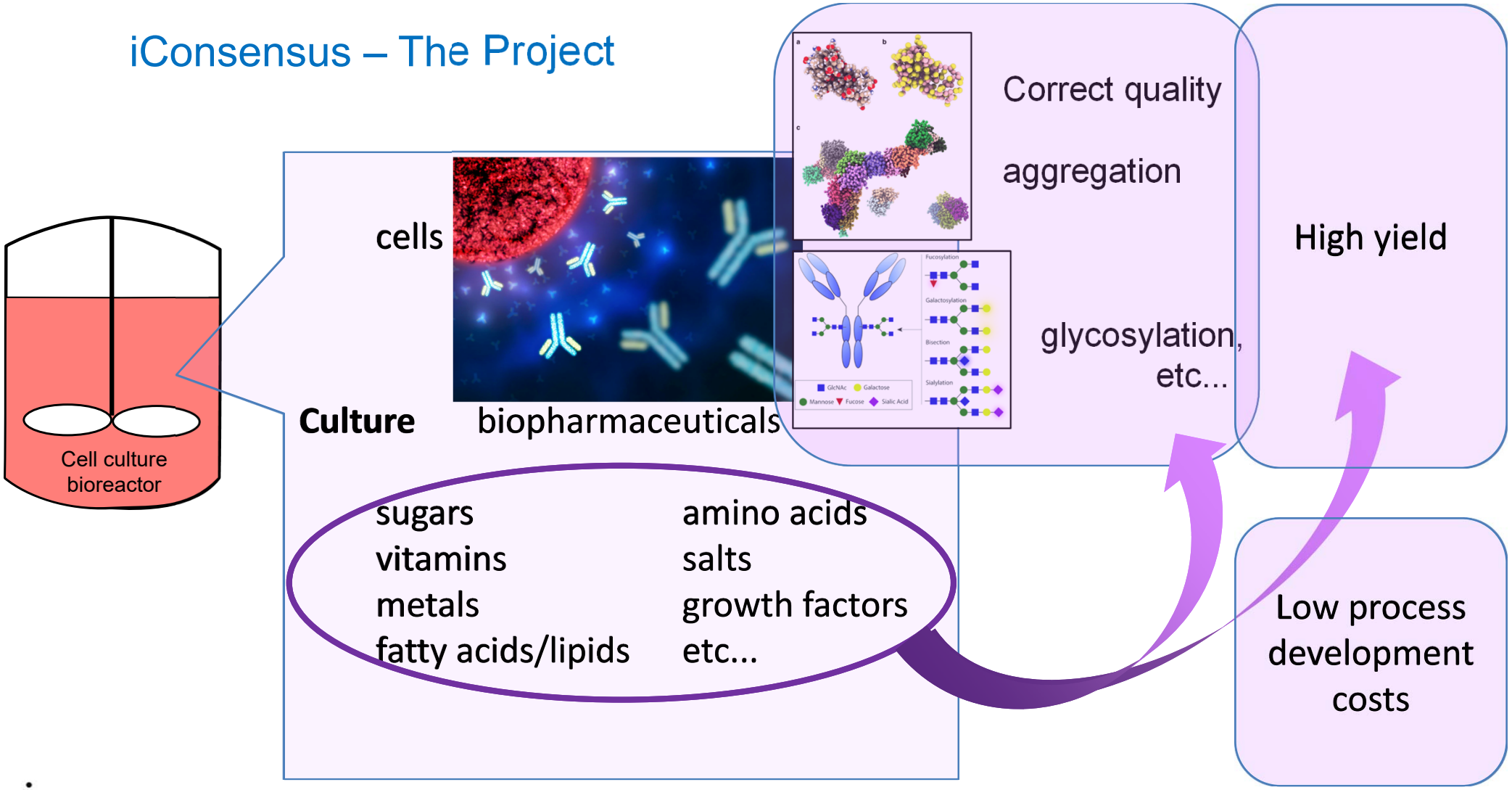
glycosylation,
etc...

Culture biopharmaceuticals

sugars	amino acids
vitamins	salts
metals	growth factors
fatty acids/lipids	etc...

Prabakaran, R., Rawat, P., Thangakani, A.M. *et al. Biophys Rev* **13**, 71–89 (2021). https://doi.org/10.1007/s12551-021-00778-w

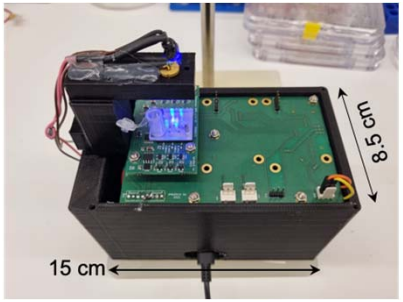
iConsensus – The Project



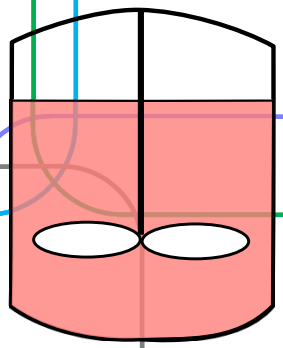
Prabakaran, R., Rawat, P., Thangakani, A.M. *et al. Biophys Rev* **13**, 71–89 (2021). https://doi.org/10.1007/s12551-021-00778-w

iConsensus – The Project = tools for on-line monitoring, for modelling and for process development

in-line miniaturised analysers

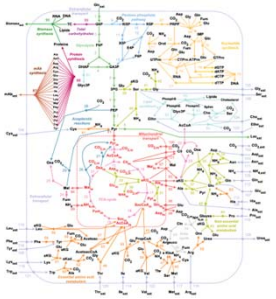


on-line probes



microbioreactors

mathematical models



iConsensus – The Project = tools for on-line monitoring, for modelling and for process development

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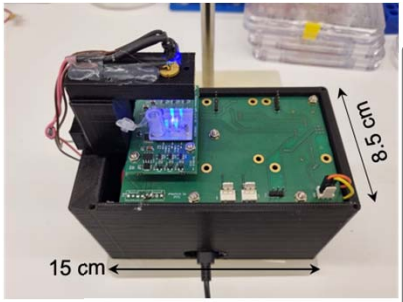
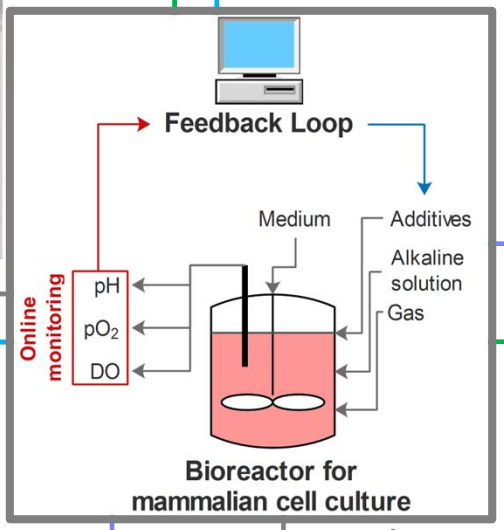
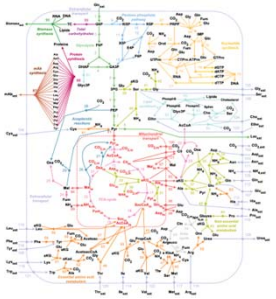


on-line probes

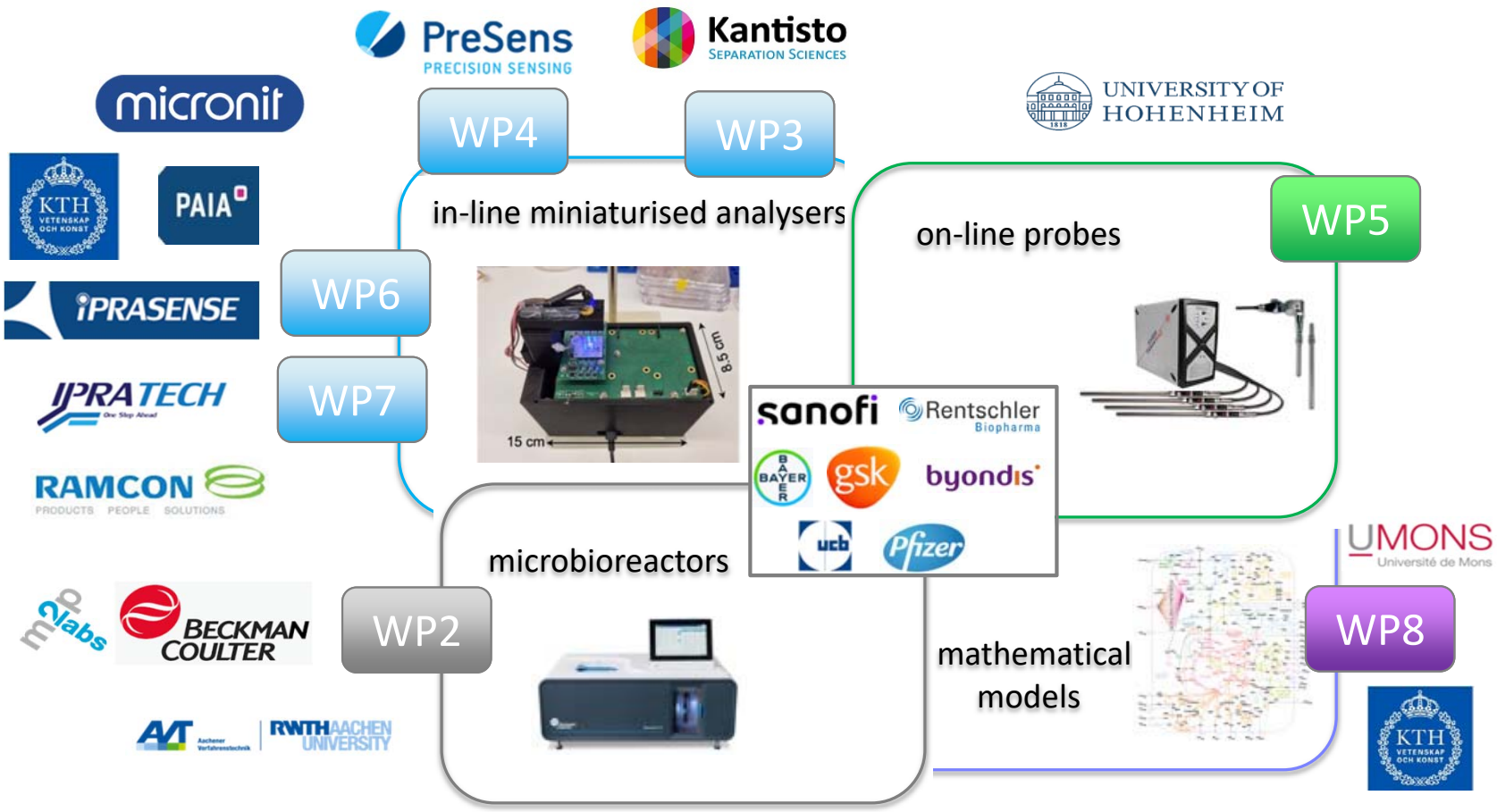


microbioreactors

mathematical models



iConsensus – The consortium of experts academia and SME's



Achievements

17 Peer reviewed publications

7 New products

28 Presentations at conferences

Attraction for new technologies

8 New technologies

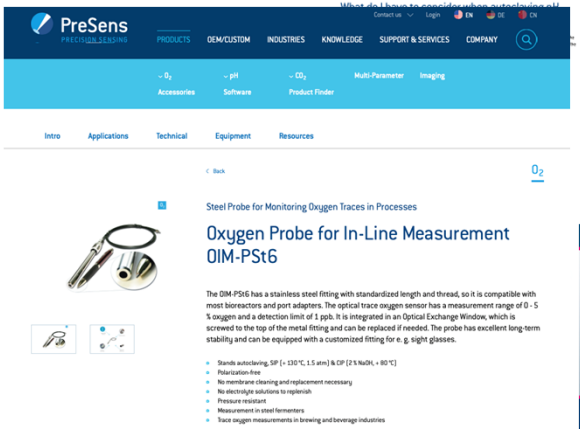
3 Patent applications

6 Application notes

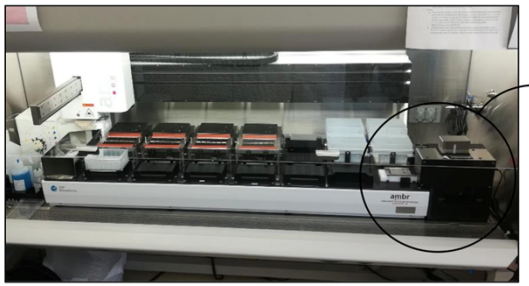
New collaborations

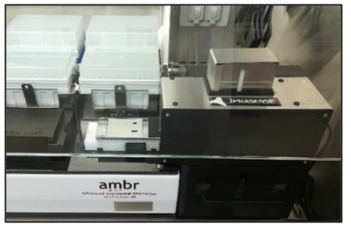
Applications in industry available today

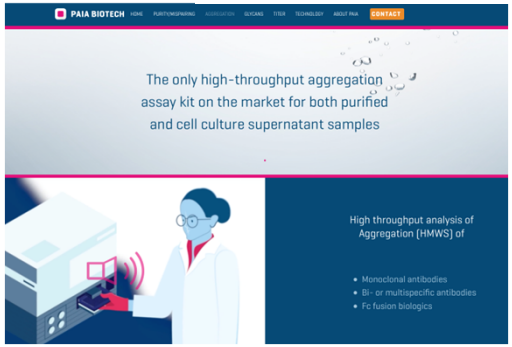
New autoclavable sensors for pH, DO, pCO2



New application of holographic-based cell density quantification







New high through-put assay for aggregation assay

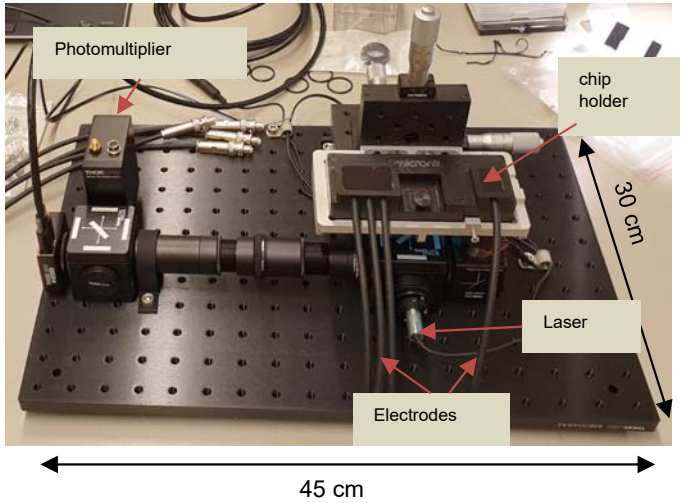
Applications in industry → further developments for commercialisation

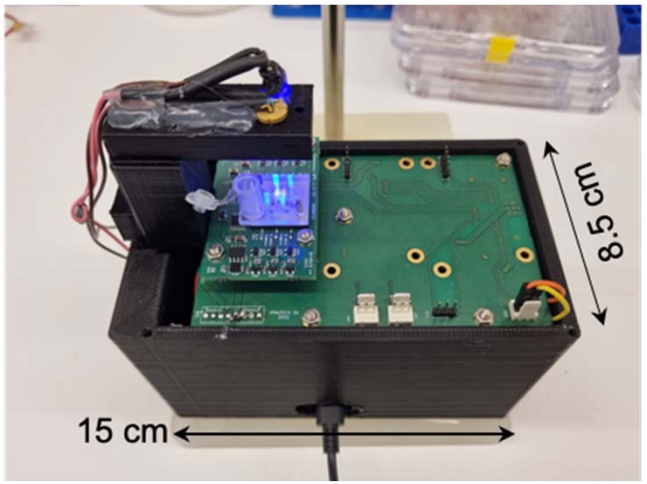
Miniaturised sensors

Proof-of-concept ✓

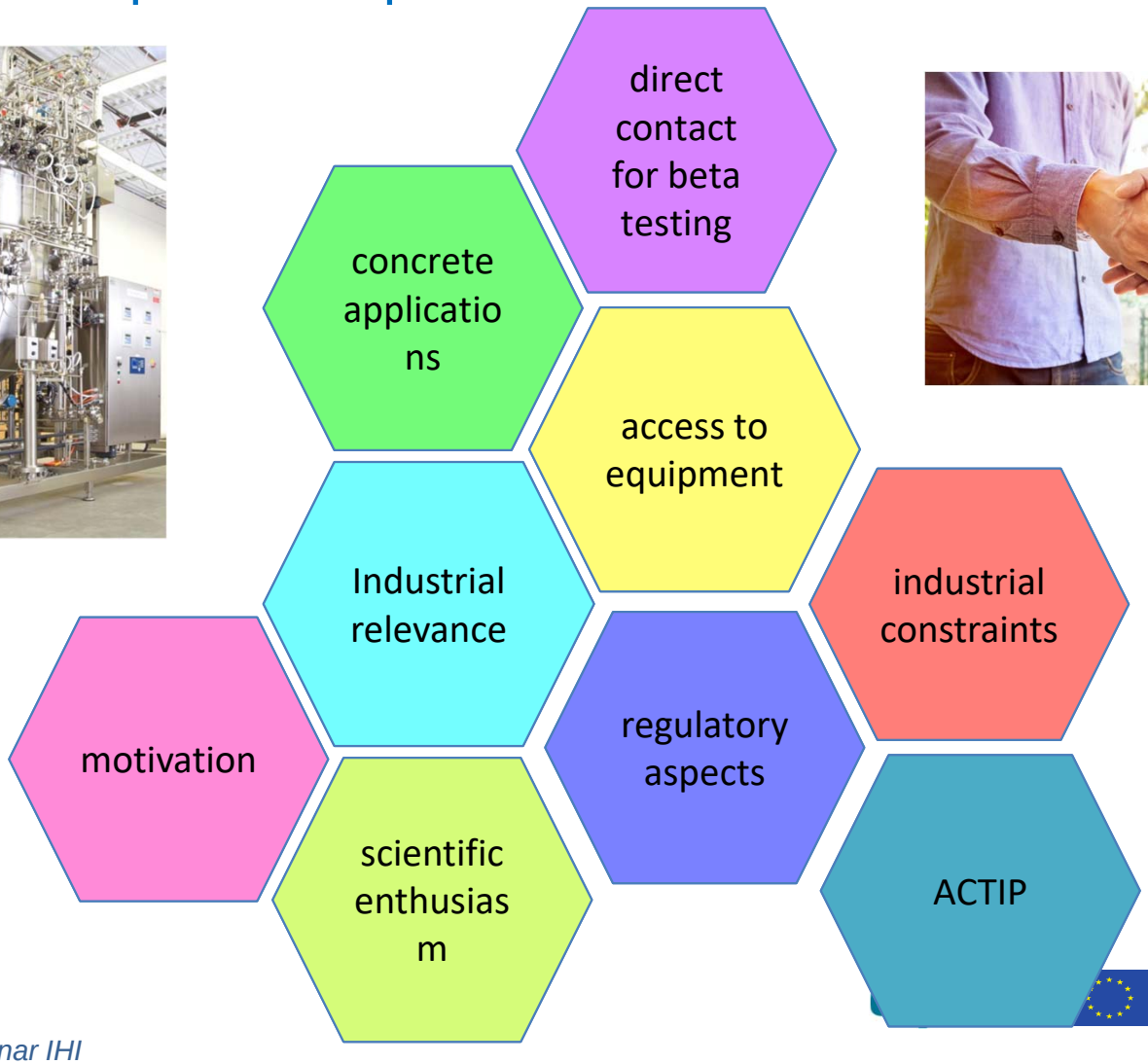
2 to 4 years

Commercialisation



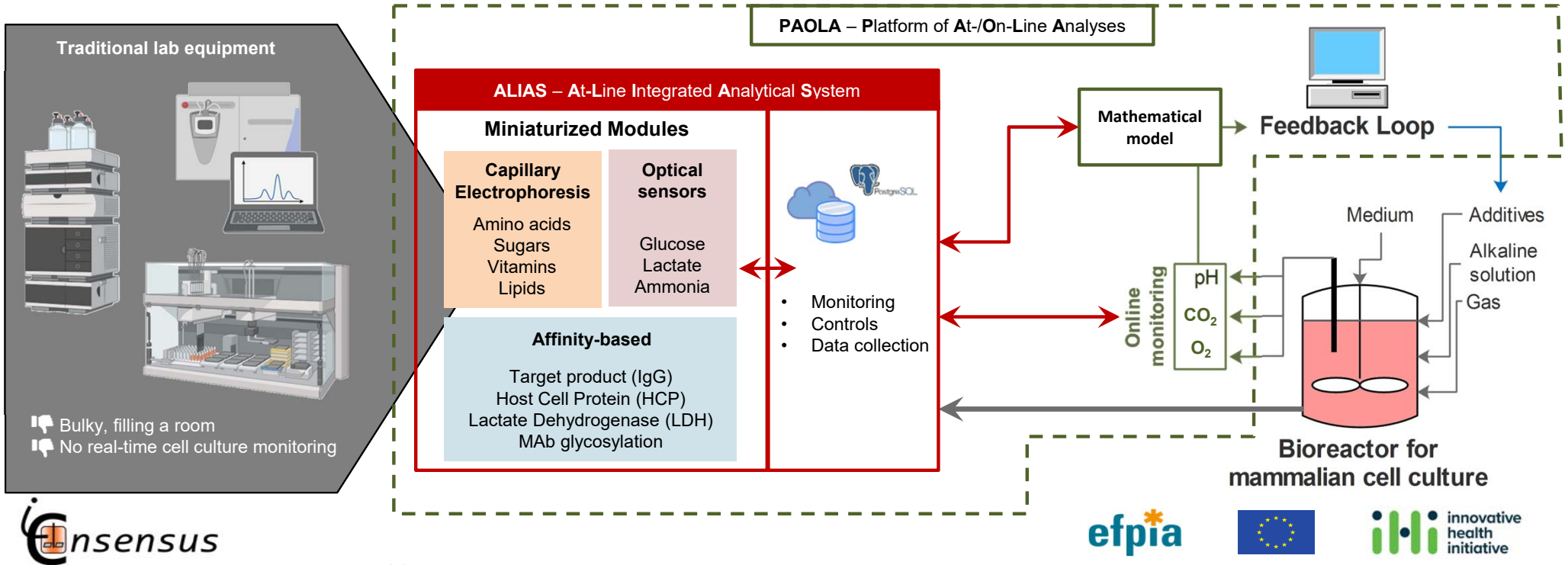


The public-private partnership to achieve iConsensus results/impact



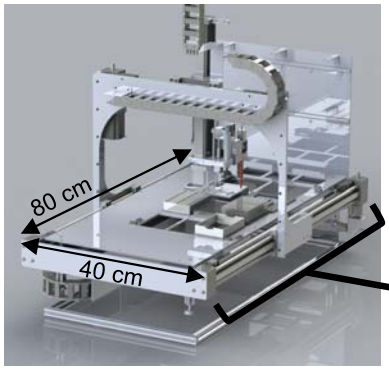
WP7 - system automation & integration, and data monitoring & management

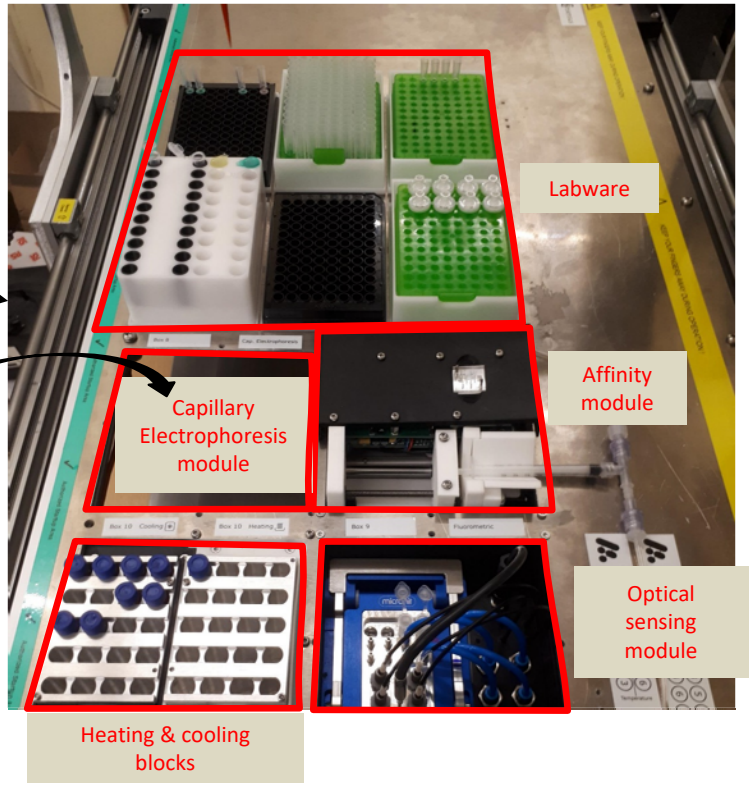
- Objective – Create an **A**t-**L**ine **I**ntegrated **A**nalytical **S**ystem (ALIAS) hosting different miniaturized analysis modules and capable of controlling, monitoring and collecting data of the **P**latform of **A**t-/**O**n-**L**ine **A**nalyses (PAOLA)

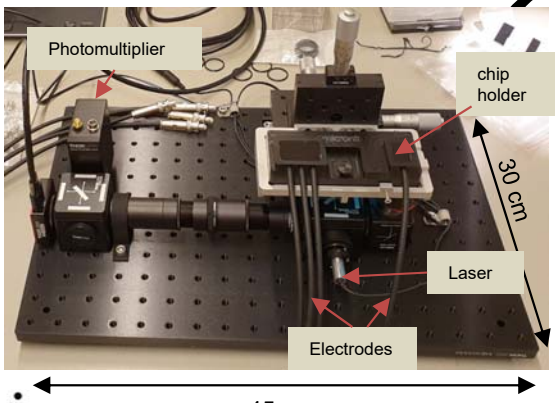


WP7 - system automation & integration, and data monitoring & management

- ALIAS: Custom liquid handler integrating 3 analyses modules…







Capabilities:

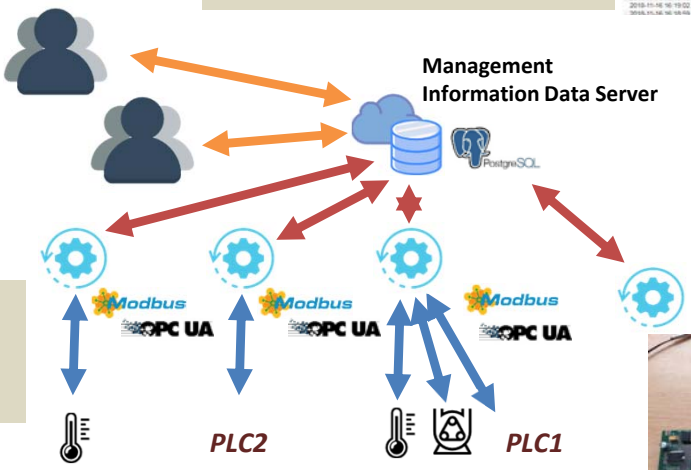
- Large range of volume handling: from 0.1 µL to 1 mL
- Sample preparation (dilution, analyte complexation)
- Reagents formulation (dilution, chemical reactions)
- Reagents storage (vials, tubes, well plates) and preservation (light protection, cooling)

WP7 - system automation & integration, and data monitoring & management

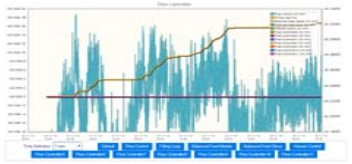
- …and electronics for automation, monitoring, control and data collection

100% Web server
Global Update/maintenance, share of data/model

Audit trail
Log of every action executed by any User on the system (to other user, planning, setup,…).
User Access control



Communication with modules, modules GUI



Multi protocols & drivers
OPC, MODBUS RTU/TCP, database import, data streaming (JSON/XML) in/out, PLCs

Electronic platform
81 channels: data acquisition or actuator connection

WP7 - system automation & integration, and data monitoring & management

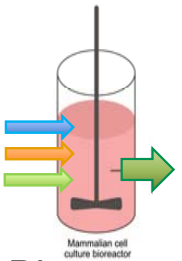
- **Integrated control and sensing platform** for biopharmaceutical cultivation process high-throughput development and production
- **ALIAS** - At-line integrated analytical system:
  - **Modular architecture** for sample/reagent preparation + analyses
  - **3 analytical modules** performing **8 analyses** (potentially up to 12)
  - **800 µL** of raw sample, **1-3** complete **analysis / day**

WP3 – CE chip platform

- Objective – analysis of culture media components and pharmaceutical product
  - Why, what, how?

- Why?
  - Correct product– safety for patients
  - Efficient manufacturing – lower cost for patients/society, sustainability

Enough but not too much nutrients for “happy cells” and efficient production?



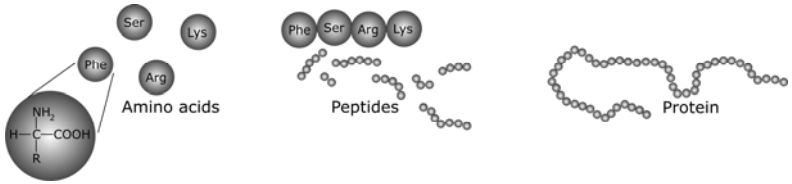
Bioreactor

Correct and safe product?

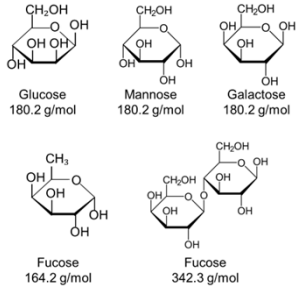
WP3 – CE chip platform

- What?
- Nutrients, products, by-products

  - Amino acids
    - The building blocks of proteins



  - Sugars and vitamins
    - Energy source, cell growth and viability

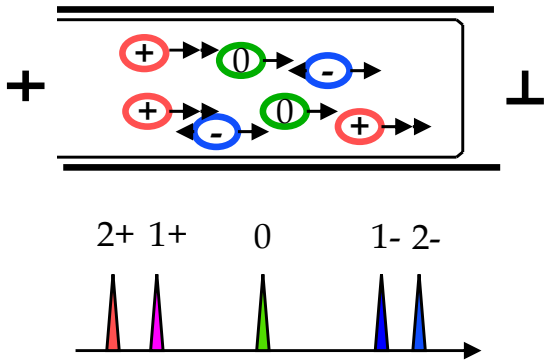


  - Product, monoclonal antibody, biopharmaceutical
    - Correct molecule, no aggregates/clusters, no fragmented products

WP3 – CE chip platform

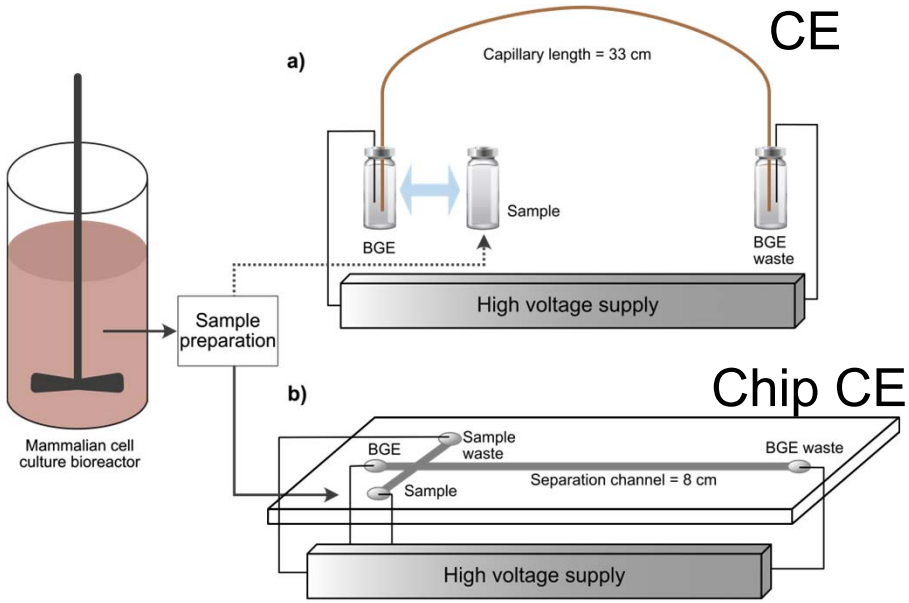
- How?
- Separation of analytes from the complex cell media

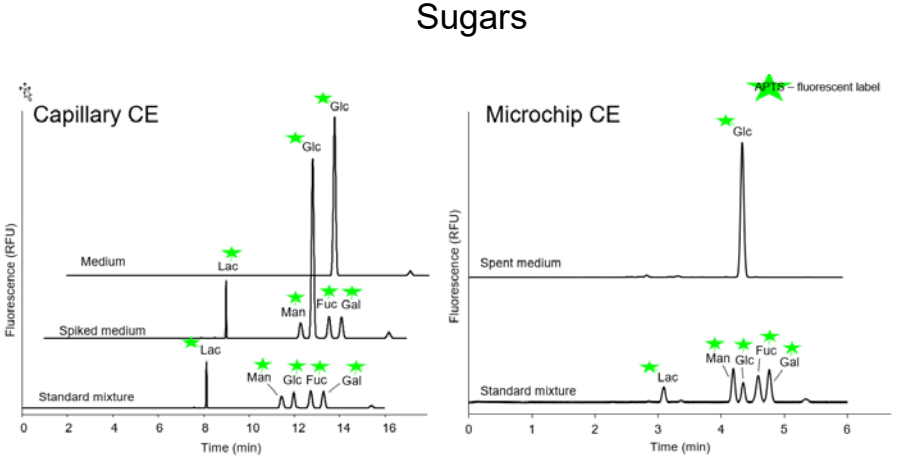
- Capillary electrophoresis, CE, and chip CE
  - Low sample volumes
  - Low consumption of chemicals
  - Low waste
  - Fast analysis
  - Small instrumentation



WP3 – CE chip platform

- How?
- CE and chip CE according to iConsensus

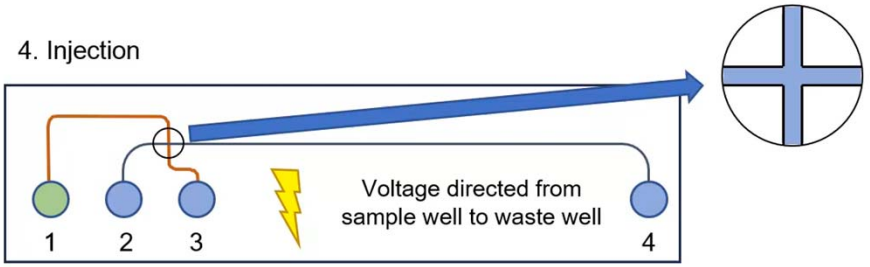




WP3 – CE chip platform

- Success? Usefulness?

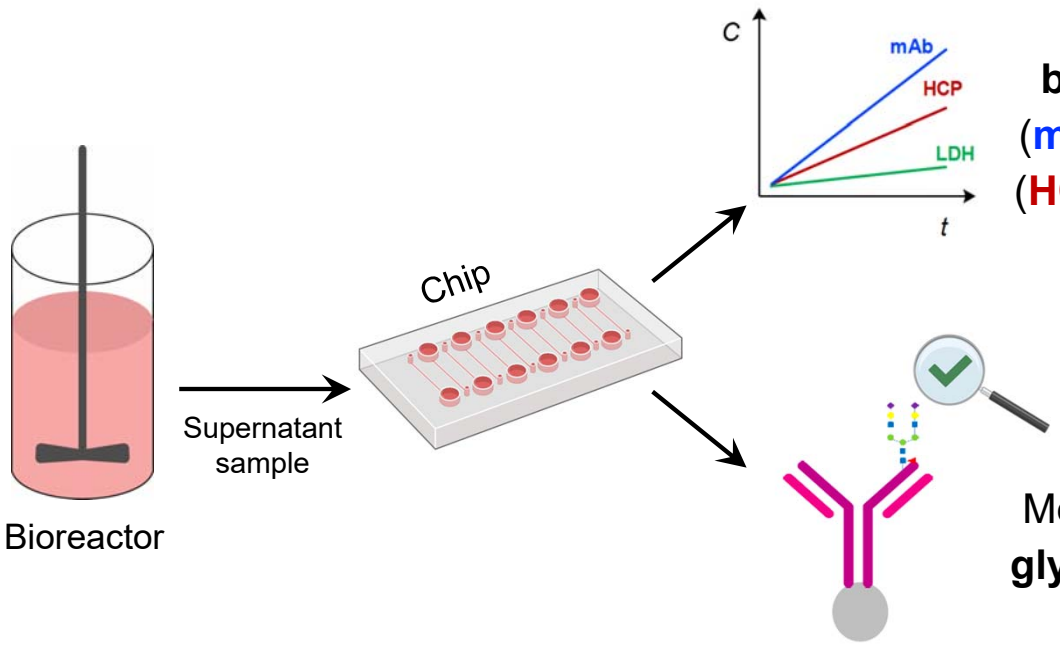
  - CE chip module working ☺
  - CE methods for ☺ :
    - amino acids
    - sugars
    - vitamins
    - product
  - CE chip methods for ☺:
    - amino acids
    - sugars
  - Used for production samples ☺
  - Tested by industrial partners ☺: Byondis, Rentschler, Sanofi



Debbie van der Burg

WP6 – Affinity-based microfluidic platform

- Objective – measurement of relevant **proteins** and pharmaceutical **product quality analysis**

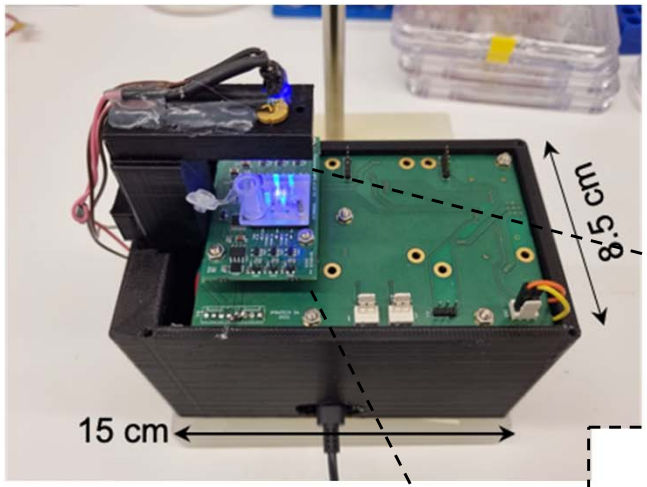


Target biopharmaceutical (**mAb**) and **impurities** (**HCP**, **LDH**) measured over time → **Efficient** manufacturing processes

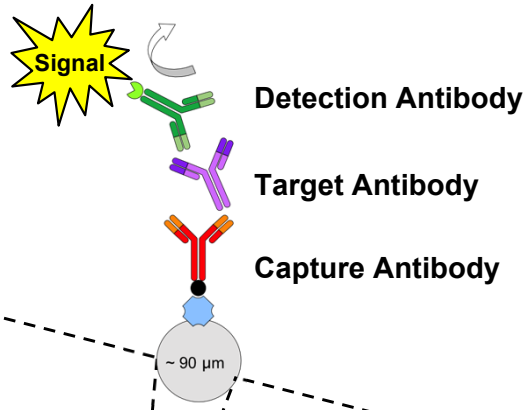
Monitoring of correct **glycosylation profile** → **Safety and efficacy** of biopharmaceutical products

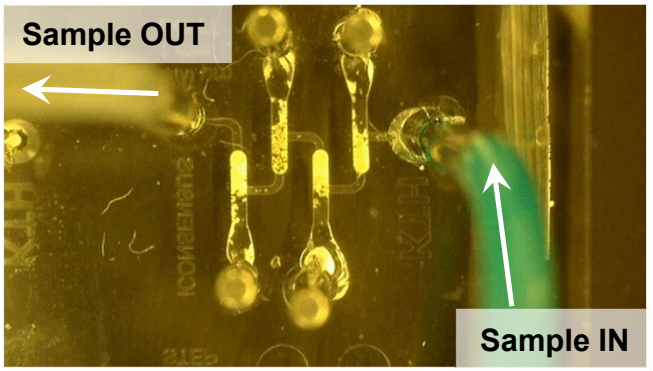
WP6 – Affinity-based microfluidic platform

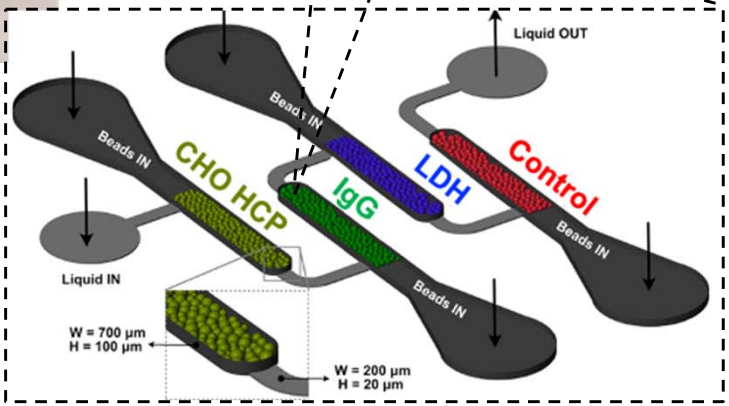
- Analysis of multiple protein targets in bioreactor samples using **immunoassays**



Module for signal readout on the chip



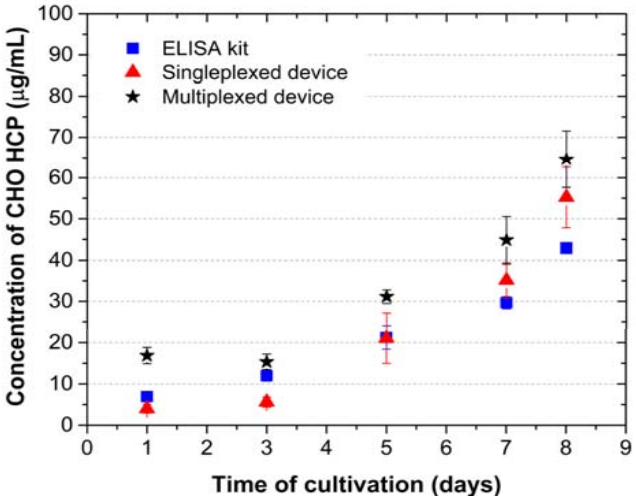




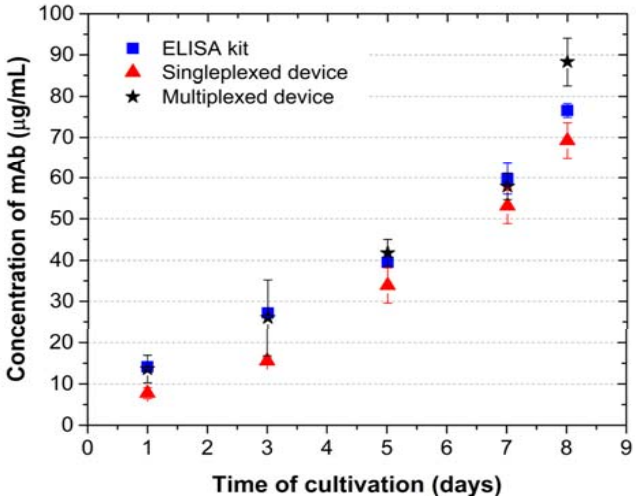
WP6 – Affinity-based microfluidic platform

- Measurement of samples from a Rituximab-producing CHO cell bioreactor

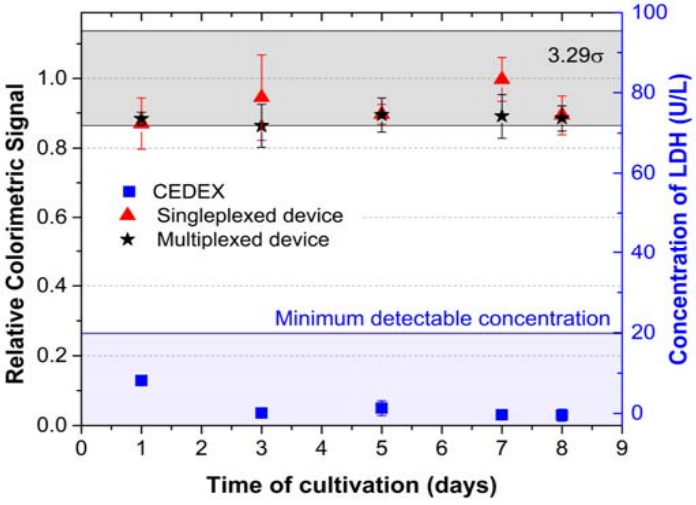
CHO HCP



mAb



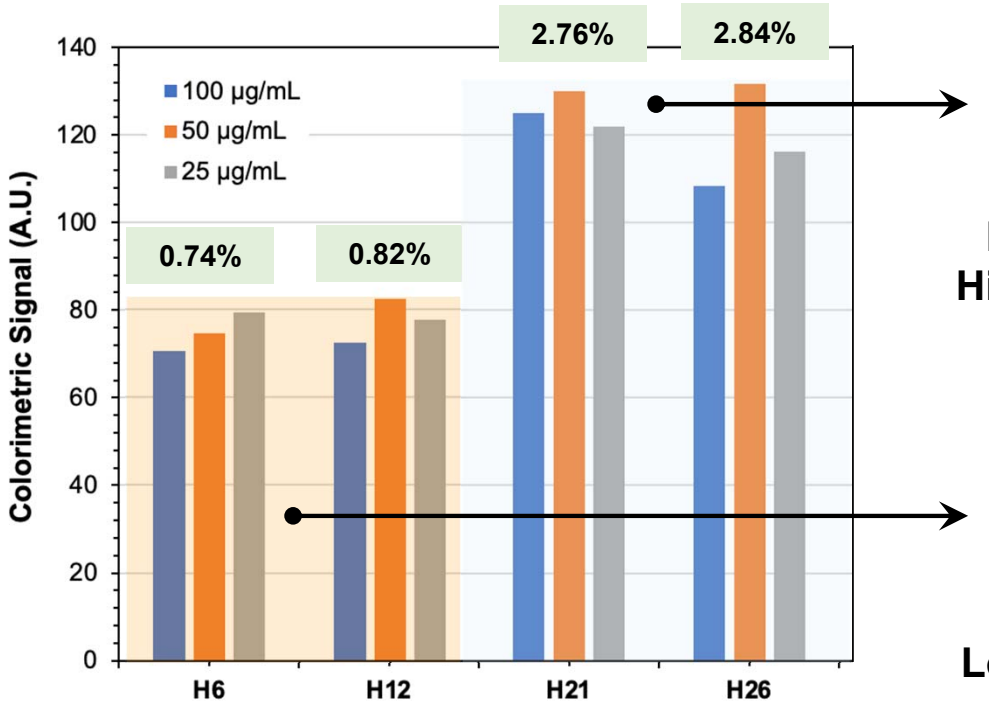
LDH



✓Good correlation between the **standard methods (■)** and the **microfluidic assays (▲,★)** developed in the scope of iConsensus

WP6 – Affinity-based microfluidic platform

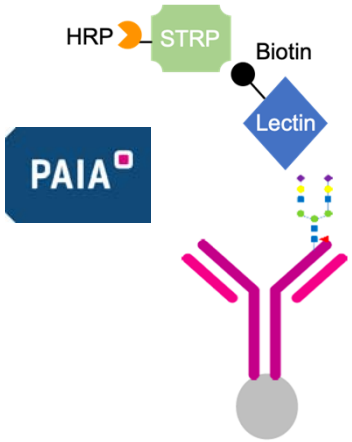
- Measurement of glycosylation in the target biopharmaceutical product



High signal
High % glycan

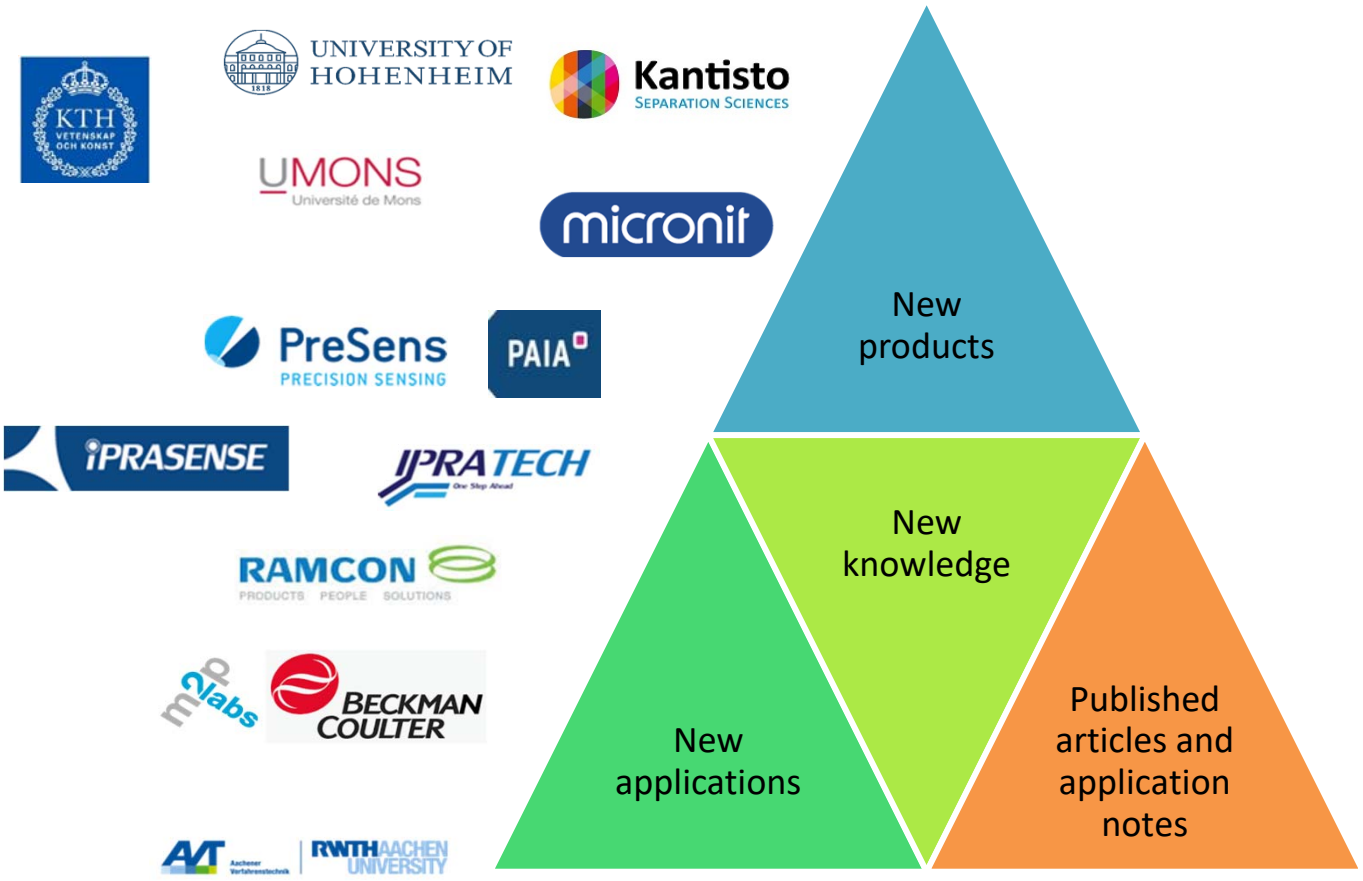
Low signal
Low % glycan

✓Measurements in the **microfluidic chip** match the **reference values (%)**



Exploitation of results and sustainability of assets developed

Exploitation of results and sustainability of assets



iConsensus peer-reviewed publications and application notes

Novel high-throughput microbioreactors for screening in mammalian cell cultures verified with CHO cells with pH and DO controls (m2p/Beckman, RWTH)

- https://publications.rwth-aachen.de/record/854042
- https://publications.rwth-aachen.de/record/825312
- https://publications.rwth-aachen.de/record/843965

New methods of capillary electrophoresis (CE), also in chip format for analysis of culture components, e.g. amino acids, sugars (KTH, Kantisto), and new CE methods for vitamins and antibody

- https://doi.org/10.1002/elps.202100122
- https://doi.org/10.1002/biot.202100325
- https://doi.org/10.1002/elps.202100213
- https://doi.org/10.1155/2022/2819855
- https://doi.org/10.1002/elps.202200144
- https://doi.org/10.1016/j.trac.2023.116975

New optical on-line sensors (Presens) with successful tests by industry

- https://www.presens.de/knowledge/publications/application-note/cell-culture-monitoring-in-stirred-tank-bioreactor-with-optical-ph-sensors-1717
- https://www.presens.de/knowledge/publications/application-note/evaluation-of-an-optical-co2-probe-for-long-term-monitoring-in-stirred-tank-bioreactors-1715
- https://www.presens.de/knowledge/publications/application-note/evaluation-of-an-optical-o2-probe-and-sensor-spots-for-long-term-measurements-in-stirred-tank-bioreactors-1713
- https://www.presens.de/knowledge/publications/application-note/online-co2-monitoring-in-cho-cell-culture-1759

Generic chemometric partial least square (PLS) prediction model (Hohenheim Univ.) to predict glucose, glutamate and lactate levels using Raman spectra from various CHO cultures and spectrometers

- doi.org/10.3390/s22155581

Prediction of amino acids and glycosylation in perfusion process (KTH)

- https://doi.org/10.1016/j.bej.2022.108426

2D fluorescence for monitoring in microtiter plates

- https://www.mdpi.com/2306-5354/9/9/438
- https://doi.org/10.1186/s13036-023-00332-0
- https://doi.org/10.3390/fermentation9020095

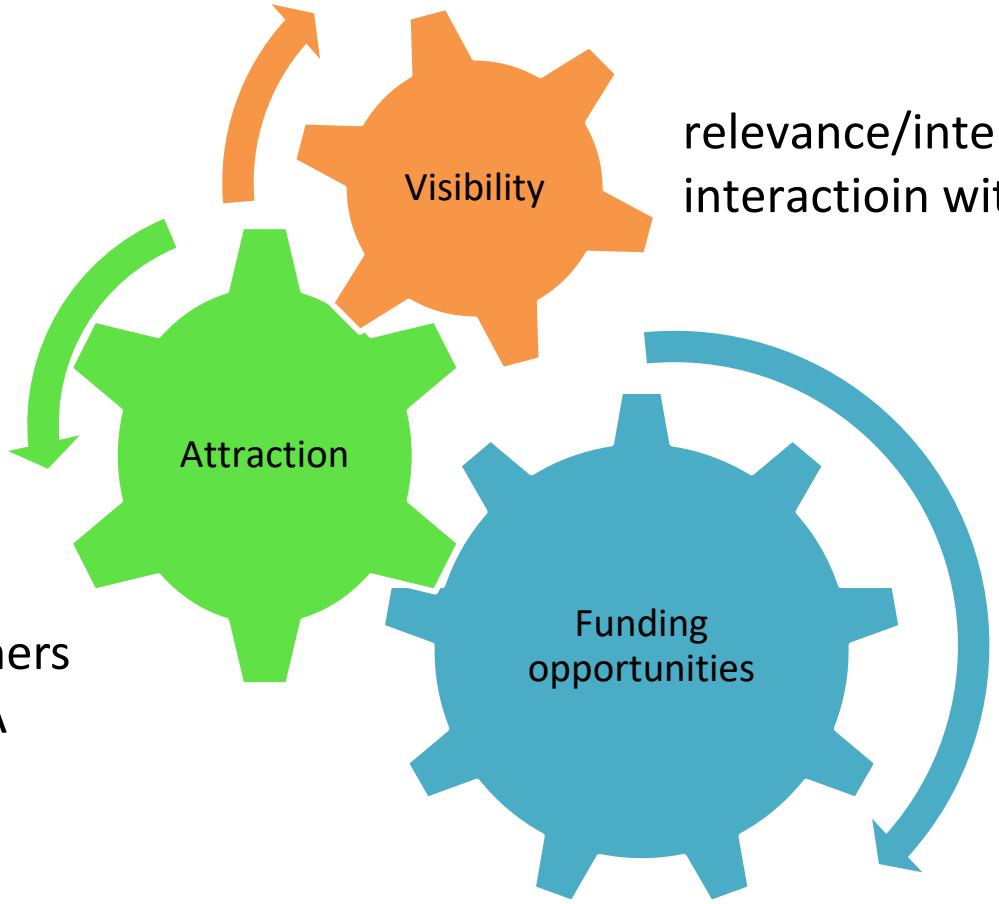
New quantification of cell density by holographic image (Iprasense), with successful test at GSK and integration to high-through put bioreactors.

- https://www.iprasense.com/wp-content/uploads/2023/02/NORMA-4S-APPLICATION-NOTE-A-fully-Automatic-Cell-Counter-for-High-Throughput.pdf
- https://www.iprasense.com/applications/viable-cell-density-monitoring-in-bioreactor/#

Novel microfluidic bead-based immunoassays validated with antibody producing CHO cell bioreactor culture (KTH), with Micronit's COC devices, for host cell proteins and antibody detections in stand-alone module (Ipratech), and fast DNA quantification by bead-based detection

- 10.1021/acssensors.0c01884
- 10.1016/j.copbio.2021.06.018

New collaborations / funding opportunities / visibility



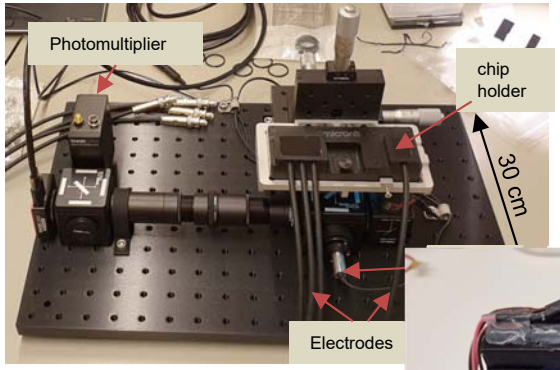
relevance/interest higher thanks to interactioin with EFPIA partners

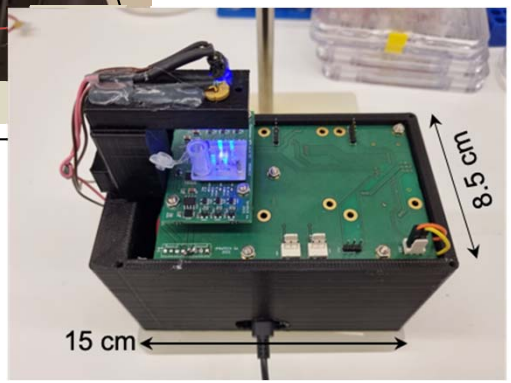
attraction for working with iConsensus academia partners → EU project 'label' , EFPIA partners 'weight'

applications for other funding applications

Further research needed to continue advancing the field

Miniaturised instruments for monitoring in process





easy operation

lower cost of goods

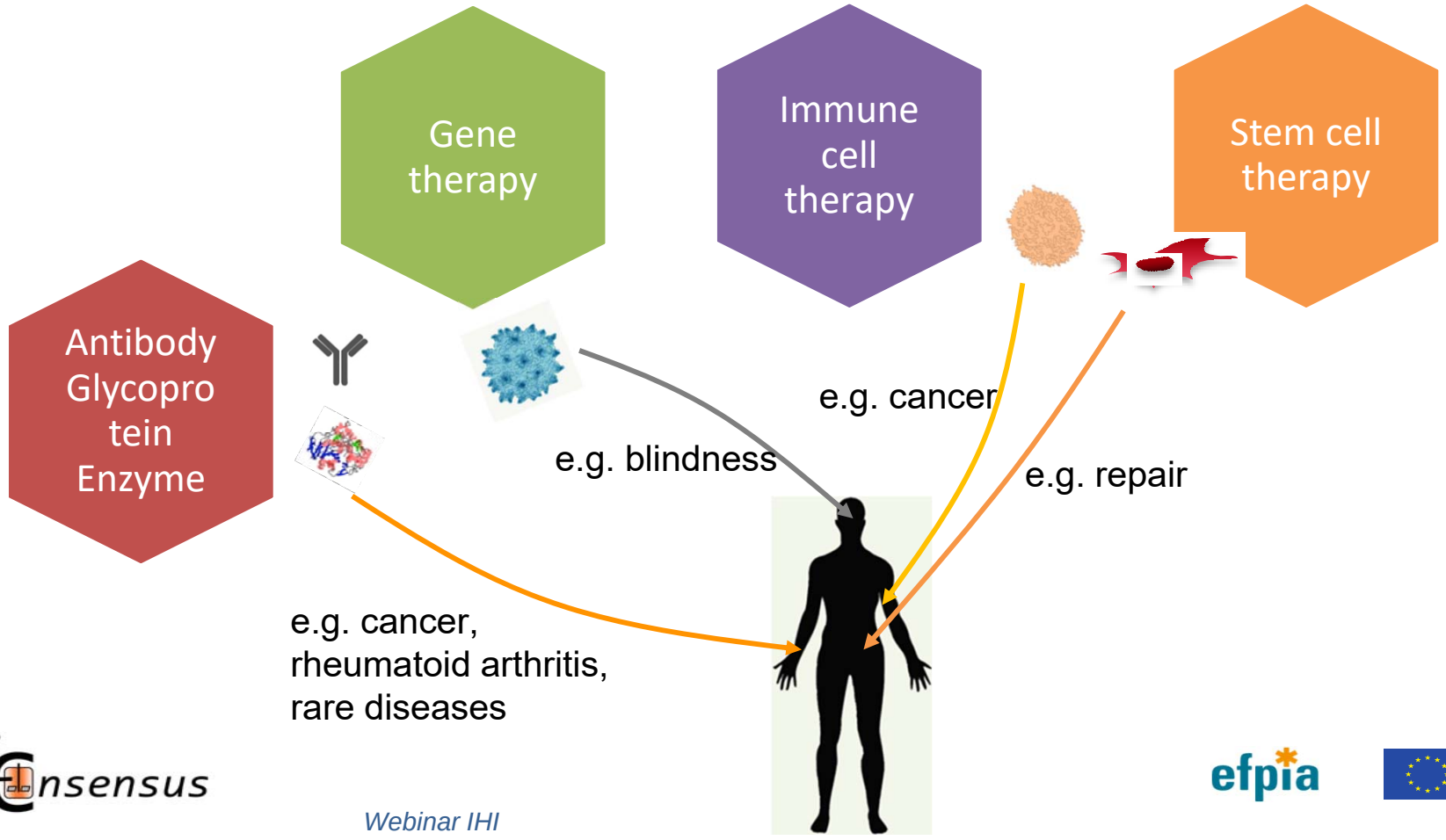
automation

simplicity

better control of process,
improved process development,
higher patient safety

Miniaturised instruments for monitoring in process

High need for bioproduction in cell and gene therapy



iConsensus in a nut-shell

iConsensus, an ambitious project, which has resulted in new products, applications and new thinking technology, from allying 19 partners, academia experts, focus-oriented SME's and industrial relevance

iConsensus

KTH Royal Institute of Technology · University of Hohenheim · UMONS Université de Mons · RWTH Aachen University

sanofi · Rentschler Biopharma · Pfizer · GSK

byondis · Bayer · ucb · PAIA

micronit · PreSens Precision Sensing · Kantisto Separation Sciences · Beckman Coulter Life Sciences · mip labs

iPRASENSE · IPRATECH Where Biotech Meets Engineering · RAMCON Products People Solutions

Innovative Medicines Initiative 2 Joint Undertaking [grant agreement No 777397]

efpia · innovative health initiative

Q&A time

Use the **chat** below to ask questions to the speakers

COCIR efpia EuropaBio MedTech Europe from diagnosis to cure Vaccines Europe Co-funded by the European Union

innovative health initiative

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Innovative Health Initiative (IHI)

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innovative health initiative

innovative health initiative

Thank you

COCIR Advancing Healthcare

efpia

EuropaBio The European Association for Bioindustries

MedTech Europe from diagnosis to cure

Vaccines Europe

Co-funded by the European Union